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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,414	12/06/2001	John Smit	08106-005001	9742

7590 06/03/2003
Fish & Richardson
225 Franklin Street
Boston, MA 02110-2804

EXAMINER

SNEDDEN, SHERIDAN

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 06/03/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/913,414

Applicant(s)

SMIT, JOHN

Examiner

Sheridan K Snedden

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 17-20 is/are rejected.
- 7) ☒ Claim(s) 1-7 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____

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DETAILED ACTION

1. Applicant's election of invention I, claims 1-15 and 17-20 and SEQ ID NO: 5 is acknowledged. Claim 16 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11, filed 01 April 2003. Claims 1-15 and 17-20 as related to SEQ ID NO: 5 are under examination.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is also referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the

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species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

Claims 1-5 are directed *Caulobacter* host cell that expresses a protein homologous to SEQ ID NO: 5 also comprising an expression vector encoding a fusion protein of a heterologous protein and a S-layer protein secretion signal, not from *C. crescentus* or SEQ ID NO: 1.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NOs: 4 and 5, the skilled artisan cannot envision the detailed chemical structure of the encompassed surface layer transport protein. Furthermore, with the exception of SEQ ID NOs: 6 or 7, the skilled artisan cannot envision the detailed chemical structure of the encompassed secretion signal. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The sequence itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

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lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated proteins comprising the amino acid sequence set forth in SEQ ID NOs: 4, 5, 6 and 7, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

3. Claims 1-15 and 17-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Caulobacter crescentus* surface layer protein secretion signals, does not reasonably provide enablement for all *Caulobacter* surface layer protein secretion signals. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention:

The nature of the invention is a host cell for use in the expression of fusion proteins.

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The breadth of the claims:

The claims are directed to *Caulobacter* host cells transformed with an expression vector. The *Caulobacter* host cells must express a protein homologous to or the same as SEQ ID NO: 5. The expression vector encodes a fusion protein of a heterologous protein linked to a *Caulobacter* surface layer protein secretion signal. Optionally, when the *Caulobacter* host cells express SEQ ID NO: 5, the secretion signal sequence is not from *Caulobacter crescentus*.

The amount of direction or guidance present and the presence or absence of working examples:

Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). In the instant case, the specification does not teach signal secretion sequence that are not a *Caulobacter* surface layer protein secretion signal but not from *Caulobacter crescentus*.

The state of the prior art and the predictability or lack thereof in the art:

The prior art teaches S-layer proteins and the secretion signal from a variety of bacterial strains (see IDS). However, of the *Caulobacter* genus, only *Caulobacter crescentus* is taught. Sequence data for all *Caulobacter* species is not taught in the art and therefore the sequence of the secretion signal from all *Caulobacter* cannot be predicted.

The quantity of experimentation needed:

The courts have interpreted undue experimentation as requiring “ingenuity beyond that to be expected of one of ordinary skill in the art” (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have

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determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). As such, the quality of experimentation necessary to identify all *Caulobacter* S-layer proteins, obtain the amino acid sequence and to determine the corresponding secretion signal is undue.

In consideration of each of factors 1 – 8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 –7 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 are directed to non-elected subject matter which render the claims indefinite. Applicant elected SEQ ID NO: 5 in the response, however, claims recite SEQ ID NO: 4.

The term "suitable" in claim 5 is a relative term which renders the claim indefinite. The term "suitable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 6 and 7 are dependent on indefinite claim 5.

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Claim 14 recites the limitation "*C. crescentus*". There is insufficient antecedent basis for this limitation in the claims the parent claims recites "protein secretion signal not present in *C. crescentus*".

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 4, 8-13, 15 and 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Smit *et al.* (US Patent 5, 550,353). Smit *et al.* teach a method of expressing S-layer(RsaA)/heterologous-protein fusion protein in a *Caulobacter* (see Claim 1). The genus of *Caulobacter* genus recited in claim 1 would inherently express proteins homologous to SEQ ID NO: 5 in both structure and function (e.g., RsaA; see column 2, lines 18-28). The *Caulobacter* host cell recited in the method is not required to be *C. crescentus* and therefore reads upon the present invention (regarding claims 1, 8-13, 15 and 19-20). Additionally, the phrase "when the cell comprises transport proteins having the same sequence as both SEQ ID NO: 4 and SEQ ID NO: 5" is interpreted as an optional limitation and not considered with regards to the reference. The DNA construct encodes a *Caulobacter* surface layer protein, or RsaA, and a heterologous protein that are both inherently linked to a secretion signal (regarding claims 8, 9, 11-13 and 19-20). The method would inherently use an operably linked promoter recognized by *Caulobacter*

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and result in the expression of the fusion protein that is displayed on the surface of the *Caulobacter* (regarding claim 4, 10, 15). Thus, the reference anticipates the claimed invention.

7. Claims 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Awram *et al.* (J Bacteriol. 1998 Jun;180(12):3062-9). Awram *et al.* teach the method of identifying *Caulobacter* for use as a host cell. The method taught by Awram *et al.* includes the steps of extracting DNA from *Caulobacter*, contacting the DNA with oligos capable of binding to SEQ ID NO: 5 (or RsaE), and determination of the hybridization by PCR amplification of the product (see page 3063; regarding claims 5 and 7). The oligo were radiolabeled for the detection step (regarding claim 6). Thus, the reference anticipates the claimed invention.

Conclusion

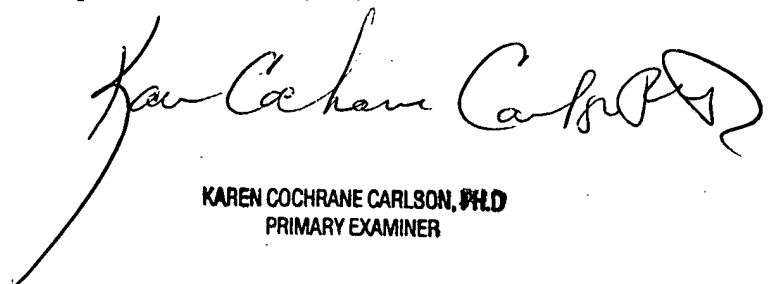
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 746-3975.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
June 2, 2003

SKS



KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER